that the lymphocyte dU suppression test may show the prior existence of folate or B_{12} deficiency as much as two months after vitamin therapy has been instituted.[7]

One can create in one's own laboratory, or purchase commercially, a kit capable of doing radioassay for both vitamin B_{12} and folic acid simultaneously, for roughly the cost and time of doing just one assay.[8]

One is inclined to agree with Carmel that the therapeutic trial is occasionally still of clinical utility. When it is done, the dose of folic acid should be 100 μg per day, and, when it is done with vitamin B_{12}, the dose should be 1 μg per day.[2]

Now that it is becoming clear that iron deficiency is present in a third to a half of all patients with megaloblastic anemia,[2] there are those who say that the old "shotgun therapy" approach was right all along. Not so. There was never anything wrong with "shotgun therapy," provided that one first made the correct diagnosis or diagnoses by appropriate testing. Such remains true today. If one draws blood for serum and red cell folate levels, serum vitamin B_{12} level, and does appropriate diagnostic tests for iron deficiency, then there is probably not much wrong with at that time starting "shotgun therapy" if one really wishes to. One can then be guided by the laboratory results as to what the deficiencies really are, and how the patient should properly be treated. "Shotgun therapy" without diagnostic evaluation first is as deplorable today as it was 40 years ago. Of course, if "shotgun therapy" is used, it may or may not be possible to diagnose a covert nutritional deficiency that is less severe than the most dominant deficiency.

Detection of malabsorption of vitamin B_{12} due to gastric or intestinal dysfunction[9] should include recognition of the important finding by Doscherholmen and Swaim[10] that the absorption of crystalline radioactive vitamin B_{12} may be normal in elderly people who subnormally absorb vitamin B_{12} from their food due to their hypochlorhydria or achlorhydria.

To the many possible causes of folate deficiency discussed by Carmel and by others,[2] must be added congenital defective transport of folate across cell walls.[11]

To the Carmel suggestion that reevaluation should be done in patients after therapy one can only say, "Amen," and add that one month after the start of vitamin therapy, reevaluation should be carried out in every patient with megaloblastic anemia for hidden iron deficiency which may only be measurable after the vitamin deficiency has been treated.[2]

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A Study of Potentially Compensable Events

ONE OF THE worthwhile results of the recent malpractice crisis in California was the decision of the California Medical Association and the California Hospital Association to sponsor the Medical Insurance Feasibility Study which is reported elsewhere in this issue. This objective study of 20,864 hospital charts from 23 representative hospitals in California developed a significant new method for measuring the frequency, causes and potential tort liability of adverse outcomes to patients in the course of health care management. The new measurement techniques which were created not only provide the most accurate information so far available, they also will be of great value in future applications.

The data are impressive. They are at once a measure of the relative safety and success of modern scientific medicine in the hospital setting where the risks are often great, but at the same

time it is sobering to realize the absolute number of misadventures that actually do occur. However, it is to some degree reassuring to find that the percentage of potentially compensable events is quite small when one realizes that all diagnosis and treatment in medicine carry a greater or lesser risk. But perhaps the greatest significance of this study is that it addresses a social, economic and very human problem of medical care in an objective and scientific fashion—and this is indeed refreshing.

—MSMW

Prognostic Determinants in Chronic Hepatitis B Infection

A Reevaluation

RATIONALES for the diagnosis and therapy of patients with chronic hepatitis have improved in recent years as serologic markers have been discovered which permit identification of the infective virus,[1] and as attempts have been made to establish standard morphologic criteria in liver biopsy specimens which would predict prognosis.[2-4] Nevertheless, despite these advances, some patients with chronic hepatitis are not readily classifiable into clinical subgroups and are perplexing diagnostic and therapeutic challenges. Usually these "problem" patients are hepatitis B surface antigen (HB_sAg)-positive since hepatitis A is frequently self-limiting and does not result in cirrhosis,[5] while patients with HB_sAg-negative chronic hepatitis most often have recognizable histologic features which predict a favorable response to corticosteroid therapy. However, in some patients with chronic HB_sAg-positive infection, the morphologic determinants of prognosis seem less reliable, and there is growing uncertainty about the efficacy of corticosteroids.[6,7]

Elsewhere in this issue, a Specialty Conference is presented from the Hepatology Division and Department of Pathology of the John Wesley County Hospital, Los Angeles, which reviews a number of clinical, epidemiologic, pathologic and therapeutic aspects of chronic hepatitis B virus (HBV) infection. This center has had an extensive experience and their long-term observations have helped to delineate some special problems that occur with this form of hepatitis, and to direct attention to additional features of this disease which may be useful in judging prognosis and choice of therapy. What are some of these problems? What determinants of prognosis are most useful clinically in the HB_sAg-positive patient? First, the findings on liver biopsy, which are generally regarded as the cornerstone of diagnosis and management in patients with all types of chronic hepatitis, may occasionally be misleading in HBV infection. They are most useful in identifying chronic persistent or unresolved viral hepatitis which are benign and nonprogressive forms of chronic HBV infection. Liver biopsy findings also readily identify patients with bridging necrosis or an advanced cirrhosis, even though sampling error may prevent accurate assessment of its extent.[8] However, in many cases the morphologic features may be more difficult to interpret. Often focal areas of portal fibrosis or nodularity are seen although there is no generalized loss of architecture. Fibrous septae may bridge portal triads in some lobules but not in others and there may be an increase in inflammatory cell infiltrate and spotty or "piecemeal" periportal necrosis and fibrosis. Usually, however, central-portal bridging is absent. The process may wax and wane with time and even vary considerably in different areas of the same biopsy specimen.[9] Pathologists usually classify this example as chronic active hepatitis according to earlier international criteria,[10] which carried with them the clinical expectation that the chronic hepatitis would progress to a cirrhosis and that the process would be arrested with steroids. The recent experience of the John Wesley Hospital hepatologists and pathologists, as well as others, is that neither of these conclusions may necessarily be correct, particularly if the patient has chronic HB_sAg-positive hepatitis.

If the liver biopsy findings cannot always be relied upon to determine prognosis, are there other clinical findings that might be helpful in identifying those patients who are likely to progress to cirrhosis? Since a young asymptomatic male with chronic active hepatitis frequently has a relatively nonprogressive illness, the patient's age and sex and whether or not he has symptoms may be important. Age has long been recognized to influence the response to hepatitis infection, although the reasons have never been fully elucidated.[11] Changes in immune response to the HBV infection or relative impairments in the regenerative response have been offered as possible explanations. Dr. Peters has called this "the impaired regeneration syndrome" emphasizing that older